01

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GI For diagram(s), see printed CA Issue.

AB 1-(Aminomethyl)cycloalkaneacetic acids I (R = Na, NH4, n = 6; R = Na, Ca, n = 7), I.HCl (R = Me, Bu, n = 6; R = Me, n = 7), I.HO3SC6H4Me-p (R = Bu, n = 5, 7), and I.HO3SPh (R = H, n = 5) were prepared as antipyretics and narcosis-potentiating agents (no data). Thus, I (R = H, n = 6) (II) was treated with an equimolar amount of 1N **NaOH** to give I (R = Na, n = 6). II.HCl was esterified with MeOH and BuOH, resp., in the presence of HCl to give I.HCl (R = Me, Bu; n = 6). The azide of 1,1-cyclopentanediacetic acid underwent a Curtius reaction to give I.HCl (R = H, n = 5) which was treated with PhSO3H to give the corresponding I.HO3SPh.

IT **60142-95-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of)

IT **60142-96-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with **sodium hydroxide**)

=> file wpix
FILE 'WPIX' ENTERED AT 17:52:34 ON 21 MAR 2007
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FILE LAST UPDATED: 19 MAR 2007 <20070319/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200719 <200719/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> New reloaded DWPI Learn File (LWPI) available as well <<<

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<

>>> New display format FRAGHITSTR available <<<
SEE ONLINE NEWS and
http://www.stn-international.de/archive/stn_online_news/fraghitstr_ex.pdf

>>> IPC Reform backfile reclassification has been loaded to 31 December 2006. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC. <<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX
PLEASE SEE
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

=> d que nos 126
L20 532 SEA FILE=WPIX ABB=ON PLU=ON GABAPENTIN OR NEURONTIN
L21 39 SEA FILE=WPIX ABB=ON PLU=ON GABAPENTIN (W) (HCL OR HYDROCHLORIDE OR (HYDROGEN OR H) (W) (CL OR CHLORIDE))
L22 QUE ABB=ON PLU=ON (NA OR K OR LI OR LITHIUM OR SODIUM OR POTASSIUM) (W) (OH OR HYDROXIDE) OR NAOH OR KOH OR LIOH OR ALKALI METAL BASE
L23 39 SEA FILE=WPIX ABB=ON PLU=ON L20 AND L21
L24 18 SEA FILE=WPIX ABB=ON PLU=ON L20 AND L21 AND L22
L25 11 SEA FILE=WPIX ABB=ON PLU=ON L23 AND (C07C0227 OR A61K000)/IC

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L26          21 SEA FILE=WPIX ABB=ON  PLU=ON  L24 OR L25


=> file japio
FILE 'JAPIO' ENTERED AT 17:52:43 ON 21 MAR 2007
COPYRIGHT (C) 2007 Japanese Patent Office (JPO)- JAPIO

FILE LAST UPDATED: 5 FEB 2007       <20070205/UP>
FILE COVERS APRIL 1973 TO OCTOBER 26, 2006

>>> GRAPHIC IMAGES AVAILABLE <<<

=> d que nos l27
L20         532 SEA FILE=WPIX ABB=ON  PLU=ON  GABAPENTIN OR NEURONTIN
L21          39 SEA FILE=WPIX ABB=ON  PLU=ON  GABAPENTIN (W) (HCL OR
                HYDROCHLORIDE OR (HYDROGEN OR H) (W) (CL OR CHLORIDE))
L27           0 SEA FILE=JAPIO ABB=ON  PLU=ON  L20 AND L21


=> file embase
FILE 'EMBASE' ENTERED AT 17:52:55 ON 21 MAR 2007
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 FILE COVERS 1974 TO 21 Mar 2007 (20070321/ED)

 EMBASE is now updated daily.  SDI frequency remains weekly (default)
 and biweekly.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que nos l28
L20         532 SEA FILE=WPIX ABB=ON  PLU=ON  GABAPENTIN OR NEURONTIN
L21          39 SEA FILE=WPIX ABB=ON  PLU=ON  GABAPENTIN (W) (HCL OR
                HYDROCHLORIDE OR (HYDROGEN OR H) (W) (CL OR CHLORIDE))
L28           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L20 AND L21


=> file biosis
FILE 'BIOSIS' ENTERED AT 17:53:07 ON 21 MAR 2007
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 March 2007 (20070321/ED)


=> d que nos l29
L20         532 SEA FILE=WPIX ABB=ON  PLU=ON  GABAPENTIN OR NEURONTIN
L21          39 SEA FILE=WPIX ABB=ON  PLU=ON  GABAPENTIN (W) (HCL OR
                HYDROCHLORIDE OR (HYDROGEN OR H) (W) (CL OR CHLORIDE))
L29           2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L20 AND L21



=> file jicst
FILE 'JICST-EPLUS' ENTERED AT 17:53:41 ON 21 MAR 2007
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FILE COVERS 1985 TO 19 MAR 2007 (20070319/ED)

The database producer has informed us that as of March 31, 2007, they
will no longer provide updates for the JICST-EPLUS file.  Therefore,
effective March 31, 2007, JICST-EPLUS will be removed from STN.
```

```
=> d que nos 131
L20         532 SEA FILE=WPIX ABB=ON  PLU=ON  GABAPENTIN OR NEURONTIN
L21          39 SEA FILE=WPIX ABB=ON  PLU=ON  GABAPENTIN (W) (HCL OR
                HYDROCHLORIDE OR (HYDROGEN OR H) (W) (CL OR CHLORIDE))
L31           0 SEA FILE=JICST-EPLUS ABB=ON  PLU=ON  L20 AND L21


=> file medline
FILE 'MEDLINE' ENTERED AT 17:53:56 ON 21 MAR 2007

 FILE LAST UPDATED: 17 Mar 2007 (20070317/UP).  FILE COVERS 1950 TO DATE.

  All regular MEDLINE updates from November 15 to December 16 have been
  added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R))
  and 2007 tree numbers.

  The annual reload will be available in early 2007.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> d que nos 132
L20         532 SEA FILE=WPIX ABB=ON  PLU=ON  GABAPENTIN OR NEURONTIN
L21          39 SEA FILE=WPIX ABB=ON  PLU=ON  GABAPENTIN (W) (HCL OR
                HYDROCHLORIDE OR (HYDROGEN OR H) (W) (CL OR CHLORIDE))
L32           0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L20 AND L21


=> file casreact
FILE 'CASREACT' ENTERED AT 17:54:05 ON 21 MAR 2007
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26, 1996), unless otherwise indicated in the original publications.

FILE CONTENT:1840 - 17 Mar 2007 VOL 146 ISS 12

New CAS Information Use Policies, enter HELP USAGETERMS for details.

************************************************************
*                                                          *
*     CASREACT now has more than 12 million reactions      *
*                                                          *
************************************************************

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.

=> d que nos 135
L1            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  GABAPENTIN/CN
L2            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  GABAPENTIN HYDROCHLORID
                E/CN
L33          16 SEA FILE=CASREACT ABB=ON  PLU=ON  L1/PRO
L34           7 SEA FILE=CASREACT ABB=ON  PLU=ON  L2/RRT
L35           6 SEA FILE=CASREACT ABB=ON  PLU=ON  L33 AND L34


=> file wpix biosis casreact
FILE 'WPIX' ENTERED AT 17:54:25 ON 21 MAR 2007
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FILE 'BIOSIS' ENTERED AT 17:54:25 ON 21 MAR 2007

FILE 'CASREACT' ENTERED AT 17:54:25 ON 21 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

=> dup rem l26 l29 l35
PROCESSING COMPLETED FOR L26
PROCESSING COMPLETED FOR L29
PROCESSING COMPLETED FOR L35
L43 26 DUP REM L26 L29 L35 (3 DUPLICATES REMOVED)
ANSWERS '1-21' FROM FILE WPIX
ANSWERS '22-23' FROM FILE BIOSIS
ANSWERS '24-26' FROM FILE CASREACT

=> d l43 1-26 ibib abs

L43 ANSWER 1 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
DUPLICATE 1
ACCESSION NUMBER: 2005-488512 [49] WPIX
DOC. NO. CPI: C2005-148840 [49]
TITLE: Preparation of **gabapentin** useful as antiepileptic drug, comprising passage of **gabapentin** salt through strong cationic exchange resin, elution of **gabapentin**, and crystallization using organic solvent
DERWENT CLASS: B05
INVENTOR: COTARCA L; GIOVANETTI R; NICOLI A; RESTELLI A
PATENT ASSIGNEE: (ZAMB-C) ZAMBON GROUP SPA
COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005058797	A1	20050630	(200549)*	EN	16[0]	
EP 1694632	A1	20060830	(200657)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005058797	A1	WO 2004-EP53470	20041214
EP 1694632	A1	EP 2004-804827	20041214
EP 1694632	A1	WO 2004-EP53470	20041214

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1694632	A1	Based on	WO 2005058797	A

PRIORITY APPLN. INFO: IT 2003-MI2456 20031216
AN 2005-488512 [49] WPIX
AB WO 2005058797 A1 UPAB: 20051223
NOVELTY - **Gabapentin** (I) is prepared by passage of salt of (I) through an ionic (strong cationic) exchange resin, elution of (I) and crystallization from organic solvent, where the regeneration of resin is carried out by partially regenerating resin through a beater constituted by inorganic acid, adding demineralized water, adding salt solution of (I), fixing salt of (I) to resin and eluting (I) using a base.
DETAILED DESCRIPTION - **Gabapentin** (I) is prepared by:
(a) the passage of salt of (I) through an ionic (strong cationic) exchange resin;
(b) elution of (I) (which has fixed onto the column); and (c) crystallization from organic solvent. Regeneration of the ionic exchange resin is carried out by: (i) partially regenerating the resin through a beater constituted by an aqueous solution of

inorganic acid in a quantity equal to a percentage of resin moles of 50-90%; (ii) adding demineralized water to separate the beater from the solution of salt of (I); (iii) adding a solution of salt of (I) and completing the resin regeneration through the acid released by fixing the salt of (I) to the resin itself; and
(iv) eluting (I) which has fixed to the resin by using a base.
An INDEPENDENT CLAIM is also included for a regeneration process of a strong cationic exchange resin used in the purification of salt of (I), comprising steps (i) - (iii).
ACTIVITY - Anticonvulsant.
No biological data given.
MECHANISM OF ACTION - None given in the source material.
USE - (I) Is useful as antiepileptic and anticonvulsant drug.
ADVANTAGE - The regeneration method considerably reduces the quantity of eluants used in the **gabapentin** synthesis process, which provides significant reduction in the time necessary to carry out the process and in the scrap disposal costs.

L43 ANSWER 2 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
DUPLICATE 2
ACCESSION NUMBER: 2004-294437 [27] WPIX
DOC. NO. CPI: C2004-112636 [27]
TITLE: Preparation of **gabapentin hydrochloride** for treating e.g. epilepsy involves reacting acetic anhydride or ammonium acetate with 1,1-cyclohexane diacetic acid to give 3,3-pentamethylene glutarimide followed by **sodium hydroxide**
DERWENT CLASS: B05
INVENTOR: BELOTTI P; FERRARI M; GHEZZI M
PATENT ASSIGNEE: (ERRE-N) ERREGIERRE SPA
COUNTRY COUNT: 105

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20040063997	A1	20040401	(200427)*	EN	3[0]	
WO 2004031126	A2	20040415	(200427)	EN		
AU 2003273930	A1	20040423	(200465)	EN		
US 6846950	B2	20050125	(200508)	EN		
EP 1558564	A2	20050803	(200551)	EN		
AU 2003273930	A8	20051027	(200624)	EN		

bad date

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20040063997	A1	US 2003-420154	20030422
AU 2003273930	A1	AU 2003-273930	20031001
EP 1558564	A2	EP 2003-757897	20031001
WO 2004031126	A2	WO 2003-EP10866	20031001
EP 1558564	A2	WO 2003-EP10866	20031001
AU 2003273930	A8	AU 2003-273930	20031001

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2003273930	A1	Based on	WO 2004031126	A
EP 1558564	A2	Based on	WO 2004031126	A
AU 2003273930	A8	Based on	WO 2004031126	A

PRIORITY APPLN. INFO: IT 2002-MI2071 20021001
AN 2004-294437 [27] WPIX
AB US 20040063997 A1 UPAB: 20060121
NOVELTY - Preparation of **gabapentin hydrochloride** (A1) involves:
(i) reacting a mixture of acetic anhydride/ammonium acetate with 1,1-cyclohexane diacetic acid to give 3,3-pentamethylene glutarimide (A2);

(ii) treating (A2) with **NaOH** in an aqueous solution up to dissolution;
(iii) dripping the obtained solution into aqueous solution of **NaOH** or sodium hypochlorite, followed by acidification with HCl.
ACTIVITY - Anticonvulsant.
MECHANISM OF ACTION - None given.
USE - For the preparation of **gabapentin hydrochloride** (claimed), which is useful for treating cerebral disorders e.g. epilepsy.
ADVANTAGE - (A1) Exhibits **gabapentin** form II with a purity measured via HPLC greater than 99.5%, a content of lactam less than 0.110% and a content of chloride anions less than 100 ppm.

L43 ANSWER 3 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
DUPLICATE 3
ACCESSION NUMBER: 2003-401177 [38] WPIX
DOC. NO. CPI: C2003-106561 [38]
TITLE: Production of **gabapentin** useful for treating e.g. epilepsy involves hydrolysis of 2-aza-spiro(4,5)decan-3-one with HCl, followed by treatment with acetone, dissolution in water, and crystallization or digestion
DERWENT CLASS: B05
INVENTOR: FORNAROLI M; PEVERALI D; VELARDI F
PATENT ASSIGNEE: (PROC-N) PROCOS SPA
COUNTRY COUNT: 2

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 6518456	B1	20030211	(200338)*	EN	5[0]	
IT 1327011	B	20050311	(200568)	IT		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6518456 B1		US 2002-170629	20020614
IT 1327011 B		IT 2001-MI2750	20011221

PRIORITY APPLN. INFO: IT 2001-MI2750 20011221
AN 2003-401177 [38] WPIX
AB US 6518456 B1 UPAB: 20060119
NOVELTY - Production and purification of **gabapentin** involves hydrolysis of 2-aza-spiro(4,5)decan-3-one with HCl, treatment of the resulting product and filtration with acetone, dissolution in water at isoelectric pH, and crystallization or digestion in the mixtures of diisopropyl ether with ethanol or methanol.
DETAILED DESCRIPTION - Preparation of 1- (aminomethyl)cyclohexyl-acetic acid (I) in pure form involves: (a) hydrolysis of 2-aza-spiro(4.5)decan-3-one with diluted aqueous HCl and recovery of the resulting 1-(aminomethyl)cyclohexyl- acetic acid hydrochloride (II) by filtration and washing on the filter with acetone;
(b) removal of the residual hydrochloric acid from the product obtained in (a) by digestion in acetone, filtration and drying;
(c) treatment of an aqueous solution of the product obtained in (b) with bases to reach the isoelectric point (pH 7.1 - 7.2), filtration of the resulting (I) and washing on the filter with aqueous ethanol; and
(d) crystallization of (I) obtained in (c) from deionized water; or
(e) digestion of (I) in the hot ethanol/diisopropyl ether or methanol/diisopropyl ether and filtration in the cold. ACTIVITY - Anticonvulsant; Cerebroprotective.
MECHANISM OF ACTION - None given.
USE - For the production and purification of **gabapentin**, which is useful in the treatment of cerebral diseases, e.g. epilepsy and of diseases typical of the elderly, since it improves brain functionality.
ADVANTAGE - The reaction times involved in the process are shorter and procedures are easier, there is no need for ion exchange resins or complex industrial apparatuses for high-pressure filtration through porous membranes, and smaller volumes are necessary

per kg of **gabapentin** obtained. **Gabapentin** is obtained in a yield, average higher than in the known processes involving the acid hydrolysis of the lactam.

L43 ANSWER 4 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-675022 [69] WPIX
DOC. NO. CPI: C2005-204807 [69]
TITLE: New cis and trans stereoisomers of 4-tert-butylgabapentin useful for treating neuro-degenerative diseases e.g. Alzheimer's disease
DERWENT CLASS: B05
INVENTOR: BALAKRISHNAN S B; HARIHARAN S; IYER V S; KARUPPIAH M P R; KRISHNAMURTHI G; KUPPANNA A; KUPPUSWAMY N; NARAYANASWAMY S; PADMANABHAN B; PREMA G V; SUBRAYASHASTRY A
PATENT ASSIGNEE: (HIKA-N) HIKAL LTD; (INDF-C) INDIAN INST SCI
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20050209332	A1	20050922	(200569)*	EN	6[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20050209332	A1 Provisional	US 2004-553565P	20040317
US 20050209332	A1	US 2005-79481	20050315

PRIORITY APPLN. INFO: US 2005-79481 20050315
US 2004-553565P 20040317
AN 2005-675022 [69] WPIX
AB US 20050209332 A1 UPAB: 20051223
NOVELTY - Cis and trans stereoisomers of 4-tert-butylgabapentin (I) are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) preparing cis and trans stereoisomers of (I); and (2) an intermediate of 4-tert-cyclohexyl-1,1-diacetic acid mono amide.
ACTIVITY - Neuroprotective; Nootropic; Tranquilizer; Anticonvulsant.
No biological data is given.
MECHANISM OF ACTION - Alpha 2-delta sub unit of calcium channel binder.
USE - For treating neuro-degenerative diseases (e.g. Alzheimer's disease) and anxiety; and as an antiepileptic drug.
ADVANTAGE - The compounds are pure isomers.

L43 ANSWER 5 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-616522 [63] WPIX
DOC. NO. CPI: C2005-185509 [63]
TITLE: Process for the conversion of **gabapentin hydrochloride** to **gabapentin** polymorphic form II comprises dissolving the **gabapentin hydrochloride** in methanol, passing a gaseous alkylamine to the resultant solution, and removing the solvent
DERWENT CLASS: B05
INVENTOR: KALYAN S; RAO M A; DIVI M K
PATENT ASSIGNEE: (KALY-I) KALYAN S; (RAOM-I) RAO M A; (DIVI-N) DIVIS LAB LTD
COUNTRY COUNT: 2

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC

US 20050187295 A1 20050825 (200563)* EN 4[0]
IN 2004000127 I4 20051202 (200612) EN

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20050187295 A1		US 2004-852743	20040524
IN 2004000127 I4		IN 2004-CH127	20040219

PRIORITY APPLN. INFO: IN 2004-CH127 20040219
AN 2005-616522 [63] WPIX
AB US 20050187295 A1 UPAB: 20051223
NOVELTY - Process for the conversion of **gabapentin hydrochloride** (A) to **gabapentin** polymorphic form II comprises dissolving (A) in methanol in which free **gabapentin** is also soluble to form a solution; passing a gaseous alkylamine or a solution in methanol to the resultant solution; and removing the solvent from the solution, and washing the residue with a solvent, to yield **gabapentin** polymorphic form II or **gabapentin** form (III).
DETAILED DESCRIPTION - Process for the conversion of **gabapentin hydrochloride** (A) to **gabapentin** polymorphic form II comprises:
(i) dissolving (A) in methanol in which free **gabapentin** is also soluble to form a solution; (ii) passing a gaseous alkylamine or a solution in methanol to the solution of step (i) until the pH is neutral at ambient temperature; and
(iii) removing the solvent from the solution of step (ii), by employing a pressure of less than 10 mm and washing the residue with a solvent in which the alkylamine hydrochloride formed in the reaction is soluble, to yield **gabapentin** polymorphic form II or **gabapentin** polymorphic form III by choosing an appropriate solvent for washing.
USE - The invention deals with the convertion of **gabapentin hydrochloride** to **gabapentin** polymorphic form II or form III.
ADVANTAGE - The process is simple and applied commercially. The process does not use ion exchange resins and tedious column chromatography. The alkyl amine used can be easily removed. The process can yield either commercially marketed form II or the form II by a simple change of solvent.

L43 ANSWER 6 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-599702 [62] WPIX
DOC. NO. CPI: C2005-180591 [62]
DOC. NO. NON-CPI: N2005-492012 [62]
TITLE: Preparation of **gabapentin** polymorph II, comprises treatment of **gabapentin hydrochloride** with a base, followed by purification from aqueous acetone
DERWENT CLASS: B05
INVENTOR: AGARWAL V K; HUBLIKAR M; PANDITA K; PATEL A M; PATEL D J; PATEL H P; PATEL P R
PATENT ASSIGNEE: (CADI-N) CADILA HEALTHCARE LTD
COUNTRY COUNT: 1

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
IN 2003000454	I3	20050211	(200562)*	EN	[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
IN 2003000454	I3	IN 2003-MU454	20030509

PRIORITY APPLN. INFO: IN 2003-MU454 20030509
AN 2005-599702 [62] WPIX
AB IN 200300454 I3 UPAB: 20051223
NOVELTY - The preparation of a **gabapentin** polymorph II involves the treatment of **gabapentin hydrochloride** with a base (such as aqueous primary-alkyl amine,

diisopropylethyl amine and aqueous **sodium hydroxide**), followed by purification from aqueous acetone. Image 0/0

L43 ANSWER 7 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-066418 [07] WPIX
DOC. NO. CPI: C2005-023277 [07]
TITLE: Preparation of **gabapentin** used as antiepileptic comprises passing **gabapentin** inorganic salt through strong cationic ionic exchange resin, eluting **gabapentin** fixed on column, concentrating and crystallizing from organic solvent
DERWENT CLASS: B05
INVENTOR: COTARCA L; GIOVANETTI R; NICOLI A
PATENT ASSIGNEE: (ZAMB-C) ZAMBON GROUP SPA
COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004113269	A1	20041229	(200507)*	EN	10[0]	
EP 1636172	A1	20060322	(200621)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004113269	A1	WO 2004-EP6513	20040617
EP 1636172	A1	EP 2004-739973	20040617
EP 1636172	A1	WO 2004-EP6513	20040617

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1636172	A1	Based on	WO 2004113269	A

PRIORITY APPLN. INFO: IT 2003-MI1247 20030620
AN 2005-066418 [07] WPIX
AB WO 2004113269 A1 UPAB: 20050707
NOVELTY - Preparation of **gabapentin** comprises passing a **gabapentin** inorganic salt through a strong cationic ionic exchange resin, eluting **gabapentin** fixed on the column with ammonia and alkaline hydroxide aqueous solution, concentrating the obtained solution and crystallizing from organic solvent. ACTIVITY - Anticonvulsant.
No biological data is given.
MECHANISM OF ACTION - None given.
USE - Used to prepare pure antiepileptic **gabapentin** .
ADVANTAGE - The process allows substitution of a relevant amount (60-70%) of ammonia with **sodium hydroxide** , which results in a reduction of draining time and costs of the ammonia solution. The eluate volume is reduced to 20% with further reduction of costs and time.

L43 ANSWER 8 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-057708 [06] WPIX
DOC. NO. CPI: C2005-019916 [06]
TITLE: New crystalline **gabapentin** Form-IV useful in the preparation of **gabapentin** Form-II and as an anticonvulsing agent for treating e.g. epilepsy and hypokinesia
DERWENT CLASS: B05
INVENTOR: CHAVA S; GORANTLA S R; INDUKURI V S; KUMAR I V S; RAMANJANEYULU G S; SATYANARAYANA C
PATENT ASSIGNEE: (MATR-N) MATRIX LAB LTD
COUNTRY COUNT: 106

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004110342	A2	20041223	(200506)*	EN	20[6]	
IN 2003000480	I4	20050304	(200555)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004110342	A2	WO 2004-IN163	20040611
IN 2003000480	I4	IN 2003-CH480	20030612

PRIORITY APPLN. INFO: IN 2003-CH480 20030612
AN 2005-057708 [06] WPIX
AB WO 2004110342 A2 UPAB: 20060121
NOVELTY - Crystalline **gabapentin** Form-IV is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) preparation of **gabapentin** Form-IV involving (a1) reacting 1,1-cyclohexane diacetic acid mono amide with alkali hypo halite solution; (b1) acidification with acid in presence of solvent; (c1) extracting the formed **gabapentin** acid salt into organic layer; (d1) separating the organic layer, drying over dehydrating agents; (e1) adding ante solvent, followed by optional cooling to precipitate the **gabapentin** acid salt and its isolation; (f1) dissolving **gabapentin** acid salts in a short chain alcohol; (g1) adjusting pH of the solution with base at 60 - 65degreesC; and (h1) cooling the reaction mass to precipitate **gabapentin** Form-IV followed by separation of the **gabapentin** Form-IV; and
(2) preparation of **gabapentin** Form-II involving the steps (a1) - (h1), converting the Form-IV into Form-II by slurrying in ethanol at a specific temperature, and separating **gabapentin** Form-II followed by drying. ACTIVITY - Anticonvulsant; Muscular-Gen.; Cerebroprotective; Tranquilizer.
MECHANISM OF ACTION - None given.
USE - In the preparation of **gabapentin** Form-II (claimed). As an anticonvulsing agent for the treatment of convulsive type cerebral disorders e.g. epilepsy, hypokinesia including fainting and other brain trauma and for producing an improvement in the cerebral functions.
ADVANTAGE - The use of the crystalline **gabapentin** Form-IV for the preparation of **gabapentin** Form-II provides new techno-economically viable process.

L43 ANSWER 9 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-795387 [78] WPIX
DOC. NO. CPI: C2004-277596 [78]
TITLE: Preparation of **Gabapentin** Form-II for the treatment of cerebral diseases e.g. epilepsy, involves neutralization of the **Gabapentin hydrochloride** solution with base at higher temperature, followed by cooling
DERWENT CLASS: B05
INVENTOR: CHAVA S; GORANTLA S R; INDUKURI V S K; SIMHADRI S
PATENT ASSIGNEE: (MATR-N) MATRIX LAB LTD
COUNTRY COUNT: 106

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004093779	A2	20041104	(200478)*	EN	16[4]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004093779	A2	WO 2004-IN101	20040416

PRIORITY APPLN. INFO: IN 2003-CH327 20030421
AN 2004-795387 [78] WPIX
AB WO 2004093779 A2 UPAB: 20050707
NOVELTY - Preparation of **Gabapentin** Form-II involves neutralization of the **Gabapentin hydrochloride** solution with a base at higher temperature, followed by cooling.
DETAILED DESCRIPTION - Preparation of **Gabapentin** Form-II involves:
(1) reacting 1,1-cyclohexane-diacetic acid monoamide with alkali hypohalite solution at -10 to 5 degrees C; (2) acidification with hydrochloric acid in the presence of an organic solvent (A1);
(3) extraction of the formed hydrochloride salt with an organic solvent (A2);
(4) separation of the organic layer and drying over dehydrating agents;
(5) precipitation of hydrochloride salt by addition of an ante solvent followed by isolation of the salt; (6) dissolution of hydrochloride salt in ethanol; (7) separation of insolubles; (8) neutralization of the filtrate with a base at 70 degrees C to liberate the corresponding free amino acid; (9) isolation of the liberated free amino acid by cooling, leaving the by-products in the mother liquor/solvent; (10) separation of the formed **Gabapentin** Form-II; (11) purification of the product by slurrying in ethanol at 60-70 degrees C; and
(12) isolation of the final product by filtration followed by drying.
ACTIVITY - Anticonvulsant; Cerebroprotective; Vulnerary; Tranquilizer.
MECHANISM OF ACTION - None given.
USE - For the preparation of **Gabapentin** Form-II, which is useful for the treatment of cerebral diseases e.g. epilepsy, hypokinesia including fainting and other brain trauma.
ADVANTAGE - The method prepares **Gabapentin** Form-II with chloride ions less than 100 ppm with respect to **Gabapentin** and without the formation of the formation of Form-III and is cost effective industrially feasible process without the multistep conversions and avoids the disadvantages associated with prior art methods. The **Gabapentin** Form-II can be prepared with substantially lactam free and very low content of chloride ions.

L43 ANSWER 10 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-431917 [40] WPIX
DOC. NO. CPI: C2004-161836 [40]
TITLE: Preparation of 1-aminomethyl-1-cyclohexaneacetic acid, useful for the treatment of epilepsy and cerebral disorder, comprises reaction of aqueous **gabapentin hydrochloride** with aqueous **alkali metal base**, precipitation and recrystallization
DERWENT CLASS: B05
INVENTOR: HARIHARAN S; HARIHARAN S H; KUPPUSWAMY N; KUPPUSWAMY N H; MARIADAS A; MARIADAS A H
PATENT ASSIGNEE: (HIKA-N) HIKAL LTD
COUNTRY COUNT: 100

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004046085	A1	20040603	(200440)*	EN	31[0]	
AU 2002356426	A1	20040615	(200470)	EN		
EP 1603863	A1	20051214	(200582)	EN		
US 20060149099	A1	20060706	(200645)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004046085	A1	WO 2002-IN224	20021120
AU 2002356426	A1	AU 2002-356426	20021120
EP 1603863	A1	EP 2002-808152	20021120
AU 2002356426	A1	WO 2002-IN224	20021120
EP 1603863	A1	WO 2002-IN224	20021120
US 20060149099	A1	WO 2002-IN224	20060209
US 20060149099	A1	US 2006-535253	20060209

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002356426 A1	Based on	WO 2004046085 A
EP 1603863 A1	Based on	WO 2004046085 A

PRIORITY APPLN. INFO: WO 2002-IN224 20021120
AN 2004-431917 [40] WPIX
AB WO 2004046085 A1 UPAB: 20060203
NOVELTY - Preparation of 1-aminomethyl-1-cyclohexaneacetic acid (**gabapentin**) (I) comprises reaction of an aqueous solution of **gabapentin hydrochloride** in water with an aqueous solution of an **alkali metal base**
followed by heating, cooling, precipitating, ageing, separating and recrystallizing.
DETAILED DESCRIPTION - Preparation of **gabapentin** (I) comprises:
(i) preparing an aqueous solution of **gabapentin hydrochloride** in water in the ratio of one part by weight of the former to 0.5-3 parts by weight of the later; (ii) preparing an aqueous solution of an **alkali metal base** in a concentration in the range of 40-50% w/w;
(iii) adding 0.08-0.3 parts by weight of the solution obtained in (ii) to 1.5-4 parts by weight of the solution obtained in (i) at 0-20 degrees C;
(iv) heating the resulting solution gradually to a temperature in the range of 50-90 degrees C; (v) gradually cooling the resulting solution to a temperature in the range of 0-15 0C to obtain a precipitate; (vi) aging the precipitate for a period in the range of 0.5 hours to 8 hours at 0-15 degrees C; (vii) separating the precipitate from the mother liquor by conventional methods; and
(viii) recrystallizing the precipitate from a mixture of IPA, methanol and water to get (I) of over 99.5 % purity and a mother liquor.
ACTIVITY - Cerebroprotective; Anticonvulsant.
MECHANISM OF ACTION - None given.
USE - (I) is useful for the treatment of epilepsy and cerebral disorder.
ADVANTAGE - (I) provides, the process is simple and economical because it uses only **sodium hydroxide** and does not require concentrations of high volumes of solvents at reduced pressure, the yield and purity of (I) is high, the starting material for the process of this invention thereby making the process more economical and does not use any ion exchange resin.

L43 ANSWER 11 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-431916 [40] WPIX
DOC. NO. CPI: C2004-161835 [40]
TITLE: Production of **gabapentin**, useful as an anticonvulsant, comprises reacting an aqueous alkaline solution of **gabapentin hydrochloride** with sulfuric acid, followed by neutralization using inorganic base
DERWENT CLASS: B05
INVENTOR: GUPTA R P; JOSHI R D; NAIK R V; RAJSHEKHAR A; SAIGAL J C
PATENT ASSIGNEE: (GLOB-N) GLOBAL BULK DRUGS & FINE CHEM PVT LTD; (GUPT-I) GUPTA R P; (JOSH-I) JOSHI R D; (NAIK-I) NAIK R V; (NICH-N) NICHOLAS PIRAMAL INDIA LTD; (RAJS-I) RAJSHEKHAR A; (SAIG-I) SAIGAL J C; (PIRA-N) PIRAMAL INDIA LTD NICHOLAS
COUNTRY COUNT: 99

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004046084	A1	20040603	(200440)*	EN	14[0]	
AU 2002356424	A1	20040615	(200470)	EN		
US 20050119503	A1	20050602	(200537)	EN		
IN 2004000300	P4	20051209	(200604)	EN		
NZ 533859	A	20061027	(200672)	EN		
EP 1727784	A1	20061206	(200680)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004046084 A1		WO 2002-IN221	20021118
AU 2002356424 A1		AU 2002-356424	20021118
NZ 533859 A		NZ 2002-533859	20021118
AU 2002356424 A1		WO 2002-IN221	20021118
US 20050119503 A1		WO 2002-IN221	20021118
IN 2004000300 P4		WO 2002-IN221	20021118
NZ 533859 A		WO 2002-IN221	20021118
IN 2004000300 P4		IN 2004-CN300	20040212
US 20050119503 A1		US 2004-497899	20040603
EP 1727784 A1		EP 2002-807696	20021118
EP 1727784 A1		WO 2002-IN221	20021118

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2002356424	A1	Based on	WO 2004046084	A
NZ 533859	A	Based on	WO 2004046084	A
EP 1727784	A1	Based on	WO 2004046084	A

PRIORITY APPLN. INFO: WO 2002-IN221 20021118
AN 2004-431916 [40] WPIX
AB WO 2004046084 A1 UPAB: 20060121
NOVELTY - Production of **gabapentin** (G1) comprises: (1) reacting an aqueous alkaline solution of **gabapentin hydrochloride** salt with sulfuric acid, followed by neutralizing with base; and
(2) filtering inorganic salts and distilling.
DETAILED DESCRIPTION - Production of **gabapentin** (G1) comprises:
(1) reacting an aqueous alkaline solution of **gabapentin hydrochloride** salt with sulfuric acid, followed by neutralizing with inorganic base; (2) filtering inorganic salts (I1) and distilling to obtain a solid (S1);
(3) dissolving (S1) in a protic solvent; (4) filtering to remove traces of (I1) followed by distillation to obtain a residue (R1); (5) adding another solvent to (R1) and (6) isolating (G1) by filtration. ACTIVITY - Anticonvulsant.
MECHANISM OF ACTION - None given.
USE - The process is for producing **gabapentin** (claimed), useful for treating cerebral diseases such as epilepsy.
ADVANTAGE - The process avoids severe conditions and/or complexities, gives a good yield, does not involve lengthy extended process steps, is cost effective; and can be carried out using simple ingredients.

L43 ANSWER 12 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-038543 [04] WPIX
DOC. NO. CPI: C2005-012759 [04]
TITLE: New **gabapentin** derivatives e.g. (1-((2-(1-aminomethyl-cyclohexyl)-acetylamino)-methyl)-cyclohexyl)-acetic acid ethyl ester useful for epilepsy and pain syndrome therapy
DERWENT CLASS: B05
INVENTOR: CHANG Y; HWANG C; HWANG C K; HWANG J; YAO C; CHANG Y L; HWANG C S; HWANG J T; YAO C N
PATENT ASSIGNEE: (INTE-N) IND TECHNOLOGY RES INST
COUNTRY COUNT: 2

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20040248811	A1	20041209	(200504)*	EN	12[0]	
TW 589176	A	20040601	(200504)	ZH		
TW 2004010679	A	20040701	(200580)	ZH		
US 7037939	B2	20060502	(200629)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20040248811 A1		US 2003-748191	20031231
TW 589176 A		TW 2002-138154	20021231
TW 2004010679 A		TW 2002-138154	20021231

PRIORITY APPLN. INFO: TW 2002-138154 20021231
AN 2005-038543 [04] WPIX
AB US 20040248811 A1 UPAB: 20060203
NOVELTY - **Gabapentin** derivatives (I) are new.
DETAILED DESCRIPTION - **Gabapentin** derivatives of formula (I) are new.
A = R2-N(R3R4), -C(O)-(CH2)m-Ar or -C(O)-(CH2)n-Het; Ar, Ar-a = phenyl (optionally substituted); Het = 4-8 member heterocyclic (optionally substituted); R3, R4 = H, -C(O)-O-C(CH3)3 or cyclohexane derivative of formula (a);
R2 = cyclohexane derivatives of formulae (b), (c) and (e), benzene derivative of formula (d) or -CH(X)-C(O)-; X = (CH2)y-Ar-a or (CH2)z-Het-a; Het-a = 6-12 member heterocyclic group; R6 = 1-10C alkyl (optionally substituted); B1 = OR1 or phenyl derivative of formula (f); R1 = H or 2-5C alkyl;
y, z = 0-2 and
m, n = 0-4.
ACTIVITY - Anticonvulsant; Analgesic.
MECHANISM OF ACTION - None given.
USE - (I) are useful for epilepsy therapy in human patients (claimed) and also in pain syndrome therapy.
ADVANTAGE - (I) has increased oral bioavailability in vivo. (I) are conjugated with several specific unnatural amino acids, which increases the hydrophobicity of the (I). The oral bioavailability of (I) was tested in rats along with **gabapentin hydrochloride** as control. The results showed that the area under curve value of (1-((2-(1-aminomethyl- cyclohexyl)-acetylamino)-methyl)-cyclohexyl)-acetic acid ethyl ester was 14.9 times higher than the **gabapentin hydrochloride**.

L43 ANSWER 13 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-041813 [04] WPIX
DOC. NO. CPI: C2004-017057 [04]
TITLE: New amino conjugate compounds used for treating e.g. epilepsy, depression, anxiety, psychosis, faintness attacks, hypokinesia and cranial disorder
DERWENT CLASS: B05
INVENTOR: BARRETT R W; CUNDY K C; GALLOP M A; SCHEUERMAN R A
PATENT ASSIGNEE: (BARR-I) BARRETT R W; (CUND-I) CUNDY K C; (GALL-I) GALLOP M A; (SCHE-I) SCHEUERMAN R A; (XENO-N) XENOPORT INC; (XENO-N) XENOPORT
COUNTRY COUNT: 101

PATENT INFO ABBR.:

PATENT NO	KIND DATE	WEEK	LA	PG	MAIN IPC
US 20030216466	A1 20031120	(200404)*	EN	39[10]	
WO 2003099338	A2 20031204	(200406)	EN		
AU 2003243180	A1 20031212	(200443)	EN		
US 7183259	B2 20070227	(200718)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20030216466	A1 Provisional	US 2002-381604P	20020517
US 20030216466	A1	US 2003-436100	20030513
AU 2003243180	A1	AU 2003-243180	20030513
WO 2003099338	A2	WO 2003-US13404	20030513

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003243180 A1	Based on	WO 2003099338 A

PRIORITY APPLN. INFO: US 2003-436100 20030513
US 2002-381604P 20020517

AN 2004-041813 [04] WPIX

AB US 20030216466 A1 UPAB: 20050527
NOVELTY - Amino conjugate compounds (I) and (II), are new.
DETAILED DESCRIPTION - Amino conjugate compounds of formula H-(NR50-(CR51R52)a-(CR53R54)b(CR55R56)c-(CR57R58)d(CR59R60)e-C(O))- (NR61-(CR62R63)f-(CR64R65)g-(CR66R67)h-C(O))-OR2 (I) and H-(NR61-(CR62R63)f-(CR64R65)g-(CR66R67)h-C(O))-(NR50-(CR51R52)a- (CR53R54)b(CR55R56)c-(CR57R58)d(CR59R60)e-C(O))-OR2 (II) and their salts are new.
a-h = 0 or 1;
R2, R3, R50 = T;
T = alkyl, alkenyl, aryl or heteroaryl (all optionally substituted), H or alkynyl;
R51 = G or R51a;
G = alkynyl, cycloalkyl or heterocyclyl (all optionally substituted) or T;
R52 = G or R52a;
R53 = G or R53a;
R54 = G or R54a;
R55 = G or R55a;
R56 = R56a or G;
R57 = R57a or G;
R58 = R58a or G;
R59 = R59a or G;
R60 = R60a or G;
R61 = alkyl, alkenyl, alkynyl, aryl or heteroaryl (all optionally substituted), or H;
R62-R67 = G, or
R50 + R51, R53 + R54 and R61 + R62 = heterocyclyl; R51a-R60a = alkylene-D, alkenylene-D, alkynylene-D, cycloalkylene-D, heterocyclylene-D, arylene-D or heteroarylene-D (all optionally substituted);
D = T1;
T1 = C(=O)-NH-CH2-C(R7)(R8)-CH2-C(=O)-O-R3, C(=O)-CH2-CH(R7)(R8)-CH2-NH2, O-C(=O)-NH-CH2-C(R7)(R8)-CH2-C(=O)-O- R3, C(=O)-O-C(R4)(R5)-O-C(=O)-NH-CH2-C(R7)(R8)-CH2-C(=O)-O-R3 or S-C(=O)-NH-CH2-CH(R7)(R8)-CH2-C(=O)-O-R3; R7, R8 = alkyl, aryl or heteroaryl (all optionally substituted), H, alkenyl, or alkynyl; R4 and R5 = alkyl, alkyloxycarbonyl, cycloalkyl, cycloalkoxycarbonyl or (hetero)aryl (all optionally substituted), H or carbamoyl, and
R7 + R8, CR4R5 R51 + R52, R53 + R54, R55 + R56, R57 + R58, R59 + R60, R62 + R63, R64 + R65 and R66 + R67 = cycloalkyl or heterocyclyl (both optionally substituted). ACTIVITY - Anticonvulsant; Antidepressant; Tranquilizer; Neuroleptic; Neuroprotective; Analgesic; Antiinflammatory; Sedative; Antipyretic; Gastrointestinal-Gen.; Endocrine-Gen.; Antialcoholic. Tests are described, but no results are given.
MECHANISM OF ACTION - None given.
USE - Used for treating epilepsy, depression, anxiety, psychosis, faintness attacks, hypokinesia, cranial disorder, neurodegenerative disorder, panic, neuropathic pain, muscular pain, skeletal pain, inflammatory diseases, insomnia, ethanol withdrawal syndrome, hot flushes, pathological disorder effecting the genitourinary and gastrointestinal tracts, overactive bladder, sexual dysfunction, irritable bowel syndrome and their symptoms (claimed).
ADVANTAGE - (I) And (II) achieve sustained therapeutic or prophylactic blood concentration of a gamma-aminobutyric acid analog or its active metabolite in the systemic circulation.

L43 ANSWER 14 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-380053 [36] WPIX
DOC. NO. CPI: C2003-100980 [36]
TITLE: Preparation of **gabapentin** useful in treatment of pathologies of central nervous systems involves reduction of (1-nitromethyl-cyclohexyl)acetonitrile
DERWENT CLASS: B05
INVENTOR: FORNAROLI M; VELARDI F
PATENT ASSIGNEE: (PROC-N) PROCOS SPA

COUNTRY COUNT: 2

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20030009055	A1	20030109	(200336)*	EN	5[0]	
US 6521788	B2	20030218	(200336)	EN		
IT 1324891	B	20041202	(200558)	IT		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20030009055	A1	US 2002-156059	20020529
IT 1324891	B	IT 2001-MI1132	20010529

PRIORITY APPLN. INFO: IT 2001-MI1132 20010529
AN 2003-380053 [36] WPIX
AB US 20030009055 A1 UPAB: 20060119
NOVELTY - Preparation of **gabapentin** (I) involves: (a) reduction of (1-nitromethyl-cyclohexyl)acetonitrile (II) to give 3-imino-2-aza-spiro(4.5)decan-2-ol (III); (b) transformation of (III) by alkali treatment into 2-hydroxy-2-aza-spiro(4.5)decan-3-one (IV); (c) reduction of (IV) to give 2-aza-spiro(4.5)decan-3-one (V); (d) hydrolysis of (V) to **gabapentin** (I).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for new compounds of formulae (III) and (IV). ACTIVITY - Central Nervous System. No biological data is given.
MECHANISM OF ACTION - None given.
USE - The process is used for the preparation of **gabapentin** (claimed) useful in treatment of pathologies of central nervous systems.
ADVANTAGE - The phosphonoacetic acid ester of previous preparative methods (US5091567) is replaced with the more convenient acetonitrile and the formation of a mixture of **gabapentin** and corresponding lactam is avoided.

L43 ANSWER 15 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-183916 [18] WPIX
CROSS REFERENCE: 2002-416672; 2002-426101; 2002-444071; 2002-479595; 2002-590470; 2002-599422; 2002-666761; 2003-148722; 2003-237935; 2003-361737; 2003-361738; 2006-056067
DOC. NO. CPI: C2003-048402 [18]
TITLE: New GABA analogs, useful for treating epilepsy, depression, anxiety, psychosis, cranial disorders, neurodegenerative disorders, panic, pain, inflammatory diseases, insomnia, gastrointestinal disorders and pain
DERWENT CLASS: B05
INVENTOR: BARRETT R W; CUNDY K C; GALLOP M; GALLOP M A; SCHEUERMAN R A; ZERANGUE N
PATENT ASSIGNEE: (BARR-I) BARRETT R W; (CUND-I) CUNDY K C; (GALL-I) GALLOP M; (GALL-I) GALLOP M A; (SCHE-I) SCHEUERMAN R A; (XENO-N) XENOPORT INC; (ZERA-I) ZERANGUE N
COUNTRY COUNT: 99

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002100344	A2	20021219	(200318)*	EN	56[3]	
US 20030181390	A1	20030925	(200364)	EN		
EP 1412324	A2	20040428	(200429)	EN		
AU 2002345638	A1	20021223	(200452)	EN		
US 20040254344	A1	20041216	(200482)	EN		
JP 2005501013	W	20050113	(200506)	JA	193	
AU 2002345638	A8	20051027	(200624)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002100344 A2		WO 2002-US18493	20020611
US 20040254344 A1	Provisional	US 2001-297732P	20010611
US 20030181390 A1	Provisional	US 2002-364619P	20020318
US 20040254344 A1	Provisional	US 2002-364619P	20020318
AU 2002345638 A1		AU 2002-345638	20020611
EP 1412324 A2		EP 2002-744288	20020611
EP 1412324 A2		WO 2002-US18493	20020611
US 20040254344 A1		WO 2002-US18493	20020611
JP 2005501013 W		WO 2002-US18493	20020611
US 20030181390 A1		US 2002-167381	20020612
JP 2005501013 W		JP 2003-503171	20020611
US 20040254344 A1		US 2004-480293	20040713
AU 2002345638 A8		AU 2002-345638	20020611

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1412324	A2	Based on	WO 2002100344	A
AU 2002345638	A1	Based on	WO 2002100344	A
JP 2005501013	W	Based on	WO 2002100344	A
AU 2002345638	A8	Based on	WO 2002100344	A

PRIORITY APPLN. INFO: US 2002-364619P 20020318
US 2001-297732P 20010611
US 2002-167381 20020612
US 2004-480293 20040713

AN 2003-183916 [18] WPIX

CR 2002-416672; 2002-426101; 2002-444071; 2002-479595; 2002-590470; 2002-599422; 2002-666761; 2003-148722; 2003-237935; 2003-361737; 2003-361738; 2006-056067

AB WO 2002100344 A2 UPAB: 20060118

NOVELTY - gamma-Amino butyric acid (GABA) analogs (I) are new.

DETAILED DESCRIPTION - gamma-Amino butyric acid (GABA) analogs of formula H-Ii-Jj-D-Kk-OH (I), their salts, hydrates and solvates are new.

I = -(NR50-(CR51R52)a-(CR53R54)b-C(O))-; J = -(NR55-(CR56R57)c-(CR58R59)d-C(O))-; K = -(NR60-(CR61R62)e-(CR63R64)f-C(O))-; a-f, i-k = 0-1;

D = N(R3)R4-C(R5)(R6)-C(R7)(R8)-C(R9)(R10)-R11; R3 = covalent bond linking the moiety derived from a GABA analog to Jj;

R4 = H; or

R4+R9 = azetidine or pyrrolidine (both optionally substituted);

R5, R6, R50, R55, R60 = alkyl, alkenyl, (hetero)aryl (all optionally substituted), H or alkynyl; R7-R10 = alkyl, (hetero)aryl (both optionally substituted), H, alkenyl or alkynyl; or

R7+R8, R51+R53, R53+R54, R56+R57, R56+R58, R58+R59, R61+R63, R63+R64 = cycloalkyl or heterocyclic ring (both optionally substituted);

R11 = C(O)R12;

R12 = covalent bond linking the moiety derived from a GABA analog to Kk; and

R51-R54, R56-R59, R61-R64 = alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, (hetero)aryl (all optionally substituted) or H; or

R50+R51, R55+R56, R60+R61 = heterocyclyl ring (optionally substituted);

provided that

(i) at least one of a or b = 1, at least one of c or d = 1, at least one of e or f = 1 and at least one of i, j or k = 1; (ii) if k = 0 then neither I nor J is derived from alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine or phenylglycine;

(iii) when R5, R6, R9, R10 = H, then R7 or R8 are not both H or both Me; and

(iv) when D = -NH-CH2-CH(phenyl)-CH2-CO2H or -NH-CH2-CH(4-chloro-phenyl)-CH2-CO2H, then I and J are not H2NCH2C(O)-, H2NCH(CH3)C(O)- or -C(O)-C(CH3)(NH-CH2-(benzofuran-2-yl))(CH2-(1H-indole-3-yl)).

An INDEPENDENT CLAIM is also included for an oral dosage form of a GABA analog involving a sustained release oral dosage form containing (I), the dosage form further

being adapted to release the compound gradually into the intestinal lumen over a period of oral administration.
ACTIVITY - Anticonvulsant; Antidepressant; Tranquilizer; Cerebroprotective; Neuroprotective; Analgesic; Antiinflammatory; Sedative; Gastrointestinal; Antialcoholic; Antiaddictive.
MECHANISM OF ACTION - None given.
USE - For treating or preventing epilepsy, depression, anxiety, psychosis, faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, panic, pain, inflammatory diseases, insomnia, gastrointestinal disorders or ethanol withdrawal syndrome, neuropathic pain, muscular pain and skeletal pain (all claimed).
ADVANTAGE - The compound achieves sustained systemic concentrations of GABA analogs following administration to animals and permits sustained therapeutic or prophylactic systemic blood concentration of GABA analog.

L43 ANSWER 16 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-537435 [57] WPIX
DOC. NO. CPI: C2002-152387 [57]
TITLE: Separation process of **gabapentin** from **gabapentin hydrochloride** comprising elimination of chloride ion by precipitating as insoluble salt
DERWENT CLASS: B05
INVENTOR: BELOTTI P; FERRARI M; GHEZZI M
PATENT ASSIGNEE: (BELO-I) BELOTTI P; (ERRE-N) ERREGIERRE SPA; (FERR-I) FERRARI M; (GHEZ-I) GHEZZI M
COUNTRY COUNT: 98

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002044123	A1	20020606	(200257)*	EN	11	[0]
AU 2002029575	A	20020611	(200264)	EN		
EP 1347951	A1	20031001	(200365)	EN		
NZ 526370	A	20030829	(200365)	EN		
BR 2001015755	A	20031230	(200409)	PT		
IT 1319674	B	20031023	(200413)	IT		
JP 2004521875	W	20040722	(200448)	JA	19	
ZA 2003004484	A	20041124	(200481)	EN	18	
US 20050049432	A1	20050303	(200517)	EN		
MX 2003004775	A1	20050101	(200564)	ES		
EP 1347951	B1	20060913	(200661)	EN		
DE 60123125	E	20061026	(200672)	DE		
MX 240416	B	20060921	(200706)	ES		
DE 60123125	T2	20070301	(200718)	DE		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002044123	A1	WO 2001-EP13953	20011129
IT 1319674	B	IT 2000-MI2608	20001201
BR 2001015755	A	BR 2001-15755	20011129
DE 60123125	E	DE 2001-623125	20011129
EP 1347951	A1	EP 2001-990454	20011129
EP 1347951	B1	EP 2001-990454	20011129
DE 60123125	E	EP 2001-990454	20011129
NZ 526370	A	NZ 2001-526370	20011129
NZ 526370	A	WO 2001-EP13953	20011129
EP 1347951	A1	WO 2001-EP13953	20011129
BR 2001015755	A	WO 2001-EP13953	20011129
JP 2004521875	W	WO 2001-EP13953	20011129
US 20050049432	A1	WO 2001-EP13953	20011129
MX 2003004775	A1	WO 2001-EP13953	20011129
EP 1347951	B1	WO 2001-EP13953	20011129
DE 60123125	E	WO 2001-EP13953	20011129

MX 240416 B	WO 2001-EP13953 20011129
AU 2002029575 A	AU 2002-29575 20011129
JP 2004521875 W	JP 2002-546493 20011129
MX 2003004775 A1	MX 2003-4775 20030529
MX 240416 B	MX 2003-4775 20030529
ZA 2003004484 A	ZA 2003-4484 20030609
US 20050049432 A1	US 2003-433241 20031113
DE 60123125 T2	DE 2001-623125 20011129
DE 60123125 T2	EP 2001-990454 20011129
DE 60123125 T2	WO 2001-EP13953 20011129

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
DE 60123125	E	Based on	EP 1347951	A
AU 2002029575	A	Based on	WO 2002044123	A
NZ 526370	A	Based on	WO 2002044123	A
EP 1347951	A1	Based on	WO 2002044123	A
BR 2001015755	A	Based on	WO 2002044123	A
JP 2004521875	W	Based on	WO 2002044123	A
MX 2003004775	A1	Based on	WO 2002044123	A
EP 1347951	B1	Based on	WO 2002044123	A
DE 60123125	E	Based on	WO 2002044123	A
MX 240416	B	Based on	WO 2002044123	A
DE 60123125	T2	Based on	EP 1347951	A
DE 60123125	T2	Based on	WO 2002044123	A

PRIORITY APPLN. INFO: IT 2000-MI2608 20001201
AN 2002-537435 [57] WPIX
AB WO 2002044123 A1 UPAB: 20060120
NOVELTY - Conversion of **gabapentin hydrochloride** (a) into **gabapentin** (1-(aminomethyl)cyclohexaneacetic acid) (b) involves:
(i) dissolution of (a) in a solvent; and (ii) addition of an amine that allows the removal of the chloride ion from the solution by precipitation of the amine hydrochloride leaving (b) in solution in free amino acid form.
USE - **Gabapentin** is used in human therapy for the treatment of cerebral disease, particularly epilepsy.
ADVANTAGE - The amine hydrochloride or (a) are absent in the alcoholic mother waters from which **gabapentin** is isolated in FORM II. HPLC purity of (b) is in excess of 99.9% and the process does not need to use facilities such as ion exchange resins, and thus is able to overcome the technical drawbacks of the prior art. The amine used in the process can also be recovered and recycled.

L43 ANSWER 17 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-590470 [63] WPIX
CROSS REFERENCE: 2002-416672; 2002-426101; 2002-444071; 2002-479595; 2002-599422; 2002-666761; 2003-148722; 2003-183916; 2003-237935; 2003-361737; 2003-361738; 2006-056067
DOC. NO. CPI: C2002-166933 [63]
TITLE: New amino acid conjugates useful for the treatment of e.g. epilepsy
DERWENT CLASS: B05; B01
INVENTOR: BARRETT R W; CUNDY K C; GALLOP M A; SHEUERMAN R A
PATENT ASSIGNEE: (XENO-N) XENOPORT INC
COUNTRY COUNT: 97

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002042414	A2	20020530	(200263)*	EN	70[1]	
AU 2002039257	A	20020603	(200263)	EN		
AU 2002239257	A8	20051013	(200611)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002042414 A2		WO 2001-US43120	20011119
AU 2002039257 A		AU 2002-39257	20011119
AU 2002239257 A8		AU 2002-239257	20011119

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002039257 A		Based on	WO 2002042414 A
AU 2002239257 A8		Based on	WO 2002042414 A

PRIORITY APPLN. INFO: US 2001-297732P 20010611
US 2000-249804P 20001117

AN 2002-590470 [63] WPIX

CR 2002-416672; 2002-426101; 2002-444071; 2002-479595; 2002-599422; 2002-666761; 2003-148722; 2003-183916; 2003-237935; 2003-361737; 2003-361738; 2006-056067

AB WO 2002042414 A2 UPAB: 20051109

NOVELTY - Amino acid conjugates (I) are new.

DETAILED DESCRIPTION - Compounds of formula H-I'i-Jj-D-K' k-OH (I) are new.

I' = -(NR50-(CR51R52)a-(CR53R54)b-C(O))-; J = -(NR55-(CR56R57)c-(CR58R59)d-C(O))-; K' = -(NR60-(CR61R62)e-(CR63R64)f-C(O))-; a - f, i - k = 0 or 1;

D = a moiety derived from GABA analog of formula R3-NR4-C(R5)(R6)-C(R7)(R8)-C(R9)(R10)-CO2H; R3 = covalent bond linking GABA to Jj; R4 = H or R4+R9 is heterocyclic ring; R5, R6 = alkyl, alkenyl, (hetero)aryl (all optionally substituted), alkynyl or H;

R7 - R10 = alkyl, (hetero)aryl (all optionally substituted), alkenyl, alkynyl or H;

R7+R8, R51+R52, R51+R53 = cycloalkyl or heterocyclic (both optionally substituted);

R50, R55, R60 = H;

R50+R51, R60+R61, R55+R56 = heterocyclic ring; R51 - R54, R56 - R64 = (cyclo)alkyl, alkenyl, alkynyl, heterocyclyl, (hetero)aryl (all optionally substituted) or H;

R56+R57, R56+R58, R58+R59, R61+R63, R63+R64 = R51+R52; provided that:

(i) at least one of a and b, c and d, and e and f is 1, and at least one of i - k is 1; and

(ii) when D is -NH-CH2-CH(Ph)-CH2-CO2H or -NH-CH2-CH(4-chlorophenyl)-CH2-CO2H, then neither I' or J are H2NCH2C(O), H2NCH(CH3)C(O)-, NH2CH2CH2C(O)- or a group of formula (a).

ACTIVITY - Anticonvulsant; Antidepressant; Tranquilizer; Analgesic; Antiinflammatory; Gastrointestinal-Gen.

MECHANISM OF ACTION - Inhibitor. Rat and PEPT1 and PEPT2 expressing CHO cell lines were prepared as described in WO0120331. Rat and human PEPT1 and PEPT2 transporter cDNAs were sub-cloned into a modified pGEM plasmid that contained 5' and 3' untranslated sequences from the Xenopus-beta-actin gene. Xenopus laevis frogs were anesthetized by immersion in tricaine (1.5 g/ml) for 15 minutes, after which oocytes were removed and digested in frog ringer solution (NaCl2 (90 mM), KCl (2 mM), MgCl2 (1 mM), NaHEPES (10 mM), pH 7.45) with collagenase (1 mg/ml) for 80 - 100 minutes. The oocytes were washed 6 times and cells were incubated at 16degreesC and each oocyte injected with RNA (10 - 20 microg) in solution (45 microl). Transport current was measured 2 - 14 days after injection and the oocytes were clamped at -60 to -90 mV. All bath and drug-containing solutions were frog ringers solution containing CaCl2. L-phenylalanine- **Gabapentin** (A) was applied for 10 - 30 seconds until the current reached steady-state level, followed by control solution. Recordings were made from single oocyte for up to 60 minutes and to compare the oocyte expressing different levels of transport activity, a saturating concentration of glycyl-sarcosine (1 mM) was used. (A) was tested for the inhibitory activity and showed an IC50 of 56 microM.

USE - In the treatment of epilepsy, faintness attacks, hypokinesia, cranial disorders, neurodegenerative disorders, depression, anxiety, panic, pain, neuropathological disorders, gastrointestinal damage, inflammation and irritable bowel disease.

ADVANTAGE - (I) Provide sustained release of systemic blood concentrations of GABA analogs and also improve intestinal absorption of poorly absorbed drugs.

L43 ANSWER 18 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-500074 [53] WPIX
DOC. NO. CPI: C2002-141574 [53]

TITLE: Production of **gabapentin** from aqueous **gabapentin hydrochloride** solution containing inorganic salts comprises treating solution with strong cationic ion-exchange resin

DERWENT CLASS: B05

INVENTOR: CANNATA V; CORCELLA F; NICOLI A

PATENT ASSIGNEE: (CANN-I) CANNATA V; (CORC-I) CORCELLA F; (NICO-I) NICOLI A; (ZAMB-C) ZAMBON GROUP SPA

COUNTRY COUNT: 32

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002034709	A1	20020502	(200253)*	EN	8[0]	
GB 2383041	A	20030618	(200340)	EN		
EP 1341749	A1	20030910	(200367)	EN		
HU 2003002602	A2	20031128	(200405)	HU		
IT 1319234	B	20030926	(200409)	IT		
US 20040068011	A1	20040408	(200426)	EN		
JP 2004512321	W	20040422	(200428)	JA	14	
ES 2206078	A1	20040501	(200430)	ES		
EP 1475366	A1	20041110	(200473)	EN		
GB 2383041	B	20041117	(200476)	EN		
ES 2206078	B1	20050801	(200551)	ES		
IN 2003000602	P4	20050415	(200560)	EN		
EP 1341749	B1	20051214	(200602)	EN		
DE 60115954	E	20060119	(200614)	DE		
ES 2254528	T3	20060616	(200641)	ES		
DE 60115954	T2	20060907	(200660)	DE		
US 20070043237	A1	20070222	(200717)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002034709	A1	WO 2001-EP11867	20011015
IT 1319234	B	IT 2000-MI2285	20001023
IN 2003000602	P4	WO 2001-EP11867	
DE 60115954	E	DE 2001-615954	20011015
DE 60115954	T2	DE 2001-615954	20011015
EP 1341749	A1	EP 2001-988708	20011015
EP 1475366	A1 Div Ex	EP 2001-988708	20011015
EP 1341749	B1	EP 2001-988708	20011015
DE 60115954	E	EP 2001-988708	20011015
ES 2254528	T3	EP 2001-988708	20011015
DE 60115954	T2	EP 2001-988708	20011015
GB 2383041	A	WO 2001-EP11867	20011015
EP 1341749	A1	WO 2001-EP11867	20011015
HU 2003002602	A2	WO 2001-EP11867	20011015
US 20040068011	A1	WO 2001-EP11867	20011015
JP 2004512321	W	WO 2001-EP11867	20011015
GB 2383041	B	WO 2001-EP11867	20011015
EP 1341749	B1	WO 2001-EP11867	20011015
DE 60115954	E	WO 2001-EP11867	20011015
DE 60115954	T2	WO 2001-EP11867	20011015
JP 2004512321	W	JP 2002-537703	20011015
ES 2206078	B1	ES 2003-50018	20011015
GB 2383041	B	GB 2003-6346	20011015
HU 2003002602	A2	HU 2003-2602	20011015
GB 2383041	A	GB 2003-6346	20030320
ES 2206078	A1	ES 2003-50018	20030328
IN 2003000602	P4	IN 2003-CN602	20030422
US 20040068011	A1	US 2003-399409	20031125
EP 1475366	A1	EP 2004-16428	20011015
EP 1341749	B1 Related to	EP 2004-16428	20040713
US 20070043237	A1 Div Ex	WO 2001-EP11867	20011015

US 20070043237 A1 Div Ex US 2003-399409 20031125
US 20070043237 A1 US 2006-390451 20060328

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1475366	A1	Div ex	EP 1341749	A
DE 60115954	E	Based on	EP 1341749	A
ES 2254528	T3	Based on	EP 1341749	A
EP 1341749	B1	Related to	EP 1475366	A
GB 2383041	A	Based on	WO 2002034709	A
EP 1341749	A1	Based on	WO 2002034709	A
HU 2003002602	A2	Based on	WO 2002034709	A
JP 2004512321	W	Based on	WO 2002034709	A
GB 2383041	B	Based on	WO 2002034709	A
EP 1341749	B1	Based on	WO 2002034709	A
DE 60115954	E	Based on	WO 2002034709	A
DE 60115954	T2	Based on	EP 1341749	A
DE 60115954	T2	Based on	WO 2002034709	A

PRIORITY APPLN. INFO: IT 2000-MI2285 20001023
AN 2002-500074 [53] WPIX
AB WO 2002034709 A1 UPAB: 20060202
NOVELTY - Production of **gabapentin** from an aqueous **gabapentin hydrochloride** solution containing inorganic salts comprises treating the solution with a strong cationic ion-exchange resin.
ACTIVITY - Anticonvulsant.
MECHANISM OF ACTION - None given.
USE - **Gabapentin** (1-aminomethylcyclohexaneacetic acid) is useful as an antiepileptic drug.
ADVANTAGE - Purification of the hydrochloride and its conversion to free **gabapentin** are performed on a large scale in a single step.

L43 ANSWER 19 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-171531 [22] WPIX
DOC. NO. CPI: C2002-052990 [22]
TITLE: **Gabapentin** for treating cerebral diseases e.g. epilepsy contains lactam and an anion of a mineral acid
DERWENT CLASS: A96; B03; B05
INVENTOR: PESACHOVICH M; PILARSKI G; PILARSKY G; SCHWARTZ E; SCHWARZ E; SINGER C
PATENT ASSIGNEE: (PESA-I) PESACHOVICH M; (PILA-I) PILARSKY G; (SING-I) SINGER C; (TEVA-N) TEVA PHARM IND LTD; (TEVA-N) TEVA PHARM USA INC
COUNTRY COUNT: 93

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001097612	A1	20011227	(200222)*	EN	26[0]	
AU 2001068426	A	20020102	(200230)	EN		
US 20020061931	A1	20020523	(200239)	EN		
EP 1289364	A1	20030312	(200320)	EN		
US 6531509	B2	20030311	(200321)	EN		
ES 2193008	T1	20031101	(200382)	ES		
CA 2410867	C	20031209	(200404)	EN		
EP 1289364	B1	20031210	(200405)	EN		
EP 1384473	A1	20040128	(200409)	EN		
DE 60101476	E	20040122	(200415)	DE		
ES 2193008	T3	20040701	(200444)	ES		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001097612 A1		WO 2001-US19100	20010615
US 20020061931 A1	Provisional	US 2000-211967P	20000616
US 6531509 B2	Provisional	US 2000-211967P	20000616
AU 2001068426 A		AU 2001-68426	20010615
CA 2410867 C		CA 2001-2410867	20010615
DE 60101476 E		DE 2001-60101476	20010615
EP 1289364 A1		EP 2001-946364	20010615
ES 2193008 T1		EP 2001-946364	20010615
EP 1289364 B1		EP 2001-946364	20010615
EP 1384473 A1	Div Ex	EP 2001-946364	20010615
DE 60101476 E		EP 2001-946364	20010615
ES 2193008 T3		EP 2001-946364	20010615
US 20020061931 A1		US 2001-880854	20010615
US 6531509 B2		US 2001-880854	20010615
EP 1289364 A1		WO 2001-US19100	20010615
CA 2410867 C		WO 2001-US19100	20010615
EP 1289364 B1		WO 2001-US19100	20010615
DE 60101476 E		WO 2001-US19100	20010615
EP 1289364 B1	Related to	EP 2003-22372	20010615
EP 1384473 A1		EP 2003-22372	20010615

FILING DETAILS:

PATENT NO	KIND	PATENT NO
ES 2193008 T1	Based on	EP 1289364 A
EP 1384473 A1	Div ex	EP 1289364 A
DE 60101476 E	Based on	EP 1289364 A
ES 2193008 T3	Based on	EP 1289364 A
AU 2001068426 A	Based on	WO 2001097612 A
EP 1289364 A1	Based on	WO 2001097612 A
CA 2410867 C	Based on	WO 2001097612 A
EP 1289364 B1	Based on	WO 2001097612 A
DE 60101476 E	Based on	WO 2001097612 A

PRIORITY APPLN. INFO: US 2000-211967P 20000616
US 2001-880854 20010615

AN 2002-171531 [22] WPIX

AB WO 2001097612 A1 UPAB: 20060119
NOVELTY - **Gabapentin** (1-(aminomethyl)-1-cyclohexaneacetic acid) contains the corresponding lactam (less than 0.5%) and an anion of a mineral acid (20 - 100 parts per million (ppm)) and after one year of storage at 250C and 60% humidity gets converted to its corresponding lactam not exceeding 0.2 weight%.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a pharmaceutical composition comprising **gabapentin** and further contains at least one adjuvant. ACTIVITY - Cerebroprotective; Anticonvulsant; Tranquilizer; and Vulnerary.
MECHANISM OF ACTION - None given.
USE - For treating cerebral diseases e.g. epilepsy, faintness attacks, hypokinesis and cranial traumas and in treating geriatric patients.
ADVANTAGE - **Gabapentin** and its pharmaceutical formulations are stable even without meeting Augart's requirements of maintaining the anion of a mineral acid less than 20 ppm.

L43 ANSWER 20 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-090802 [10] WPIX
DOC. NO. CPI: C2001-026608 [10]
TITLE: Preparation of **gabapentin** from **gabapentin hydrochloride**, useful for the treatment of cerebral diseases such as epilepsy, hypokinesia, and cranial traumas
DERWENT CLASS: A88; B05
INVENTOR: CARACCIA N; GIORDANI C; TENCONI F
PATENT ASSIGNEE: (BIOI-N) BIOINDUSTRIA LAB ITAL MEDICINALI SPA; (CARA-I) CARACCIA N

COUNTRY COUNT: 89

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2000058268	A1	20001005	(200110)*	EN	14[0]	
AU 2000032904	A	20001016	(200110)	EN		
EP 1165489	A1	20020102	(200209)	EN		
IT 1311984	B	20020322	(200252)	IT		
US 6576790	B1	20030610	(200340)	EN		
EP 1165489	B1	20030820	(200356)	EN		
DE 60004652	E	20030925	(200371)	DE		
ES 2204533	T3	20040501	(200431)	ES		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000058268	A1	WO 2000-EP2345	20000316
IT 1311984	B	IT 1999-MI625	19990326
AU 2000032904	A	AU 2000-32904	20000316
DE 60004652	E	DE 2000-60004652	20000316
EP 1165489	A1	EP 2000-910850	20000316
EP 1165489	B1	EP 2000-910850	20000316
DE 60004652	E	EP 2000-910850	20000316
ES 2204533	T3	EP 2000-910850	20000316
EP 1165489	A1	WO 2000-EP2345	20000316
US 6576790	B1	WO 2000-EP2345	20000316
EP 1165489	B1	WO 2000-EP2345	20000316
DE 60004652	E	WO 2000-EP2345	20000316
US 6576790	B1	US 2002-937378	20020225

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 60004652	E	Based on	EP 1165489 A
ES 2204533	T3	Based on	EP 1165489 A
AU 2000032904	A	Based on	WO 2000058268 A
EP 1165489	A1	Based on	WO 2000058268 A
US 6576790	B1	Based on	WO 2000058268 A
EP 1165489	B1	Based on	WO 2000058268 A
DE 60004652	E	Based on	WO 2000058268 A

PRIORITY APPLN. INFO: IT 1999-MI625 19990326
AN 2001-090802 [10] WPIX
AB WO 2000058268 A1 UPAB: 20050705
NOVELTY - A new process for the preparation of **gabapentin** (GP) comprises adjusting an aqueous solution of GP HCl to the GP isoelectric point, diafiltering and concentrating the retentate, evaporation and precipitation.
DETAILED DESCRIPTION - A novel process for the preparation of GP starting from GP HCl comprises:
(a) preparing a GP HCl aqueous solution; (b) adjusting the pH of the solution to or about to GP isoelectric point by addition of a basic compound comprising a monovalent anion;
(c) diafiltering the solution through a membrane highly selective for organic compounds with molecular weight (MW) higher than 150 and poorly selective for inorganic monovalent ions, to separate the solution into an aqueous permeate containing chloride ions and a retentate containing unsalified GP free from chloride ions;
(d) concentrating the retentate by increasing the pressure exerted on the membrane to obtain a concentration of unsalified GP in the retentate of at least 5%;
(e) evaporating the retentate under reduced pressure below 35degreesC; and
(f) precipitating GP by addition of an alcohol. ACTIVITY - Cerebroprotective; Anticonvulsant; Tranquilizer; Vulnerary.
MECHANISM OF ACTION - None given.

USE - The GP is used for the treatment of various cerebral diseases, e.g. epilepsy, hypokinesia, or cranial traumas, (see US4024175 and US4087544).
ADVANTAGE - The process provides a simple technique which requires no drastic operative conditions, such as high temperatures, which would cause the undesired formation of the GP lactam.

L43 ANSWER 21 OF 26 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-254361 [21] WPIX
DOC. NO. CPI: C1999-074378 [21]
TITLE: Stereoselective preparation of **gabapentin**
DERWENT CLASS: B05
INVENTOR: BRYANS J S; MORRELL A I
PATENT ASSIGNEE: (WARN-C) WARNER LAMBERT CO; (WARN-C) WARNER LAMBERT CO LLC
COUNTRY COUNT: 72

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 9914184	A1	19990325	(199921)*	EN	22[0]	
ZA 9808508	A	19990630	(199931)	EN	21	
AU 9887791	A	19990405	(199933)	EN		
EP 1015415	A1	20000705	(200035)	EN		
NO 2000001404	A	20000317	(200035)	NO		
BR 9812351	A	20000919	(200050)	PT		
MX 2000000063	A1	20000501	(200129)#	ES		
HU 2000004582	A2	20010528	(200140)	HU		
KR 2001024079	A	20010326	(200161)	KO		
JP 2001516738	W	20011002	(200172)	JA	23	
NZ 502786	A	20020531	(200246)	EN		
US 6465689	B1	20021015	(200271)	EN		
AU 752444	B	20020919	(200272)	EN		
EP 1015415	B1	20030507	(200333)	EN		
DE 69814420	E	20030612	(200346)	DE		
ES 2197493	T3	20040101	(200412)	ES		
CA 2295993	C	20040504	(200431)	EN		
MX 218160	B	20031215	(200470)	ES		
PH 1199802410	B1	20031010	(200560)	EN		
KR 563894	B1	20060324	(200705)	KO		
JP 3878809	B2	20070207	(200713)	JA	14	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9914184 A1		WO 1998-US16652	19980811
US 6465689 B1	Provisional	US 1997-59204P	19970918
AU 9887791 A		AU 1998-87791	19980811
AU 752444 B		AU 1998-87791	19980811
BR 9812351 A		BR 1998-12351	19980811
CA 2295993 C		CA 1998-2295993	19980811
DE 69814420 E		DE 1998-614420	19980811
EP 1015415 A1		EP 1998-939340	19980811
EP 1015415 B1		EP 1998-939340	19980811
DE 69814420 E		EP 1998-939340	19980811
ES 2197493 T3		EP 1998-939340	19980811
NZ 502786 A		NZ 1998-502786	19980811
EP 1015415 A1		WO 1998-US16652	19980811
NO 2000001404 A		WO 1998-US16652	19980811
BR 9812351 A		WO 1998-US16652	19980811
HU 2000004582 A2		WO 1998-US16652	19980811
JP 2001516738 W		WO 1998-US16652	19980811
NZ 502786 A		WO 1998-US16652	19980811
US 6465689 B1		WO 1998-US16652	19980811
EP 1015415 B1		WO 1998-US16652	19980811

DE 69814420 E	WO 1998-US16652 19980811
CA 2295993 C	WO 1998-US16652 19980811
MX 218160 B	WO 1998-US16652 19980811
KR 563894 B1	WO 1998-US16652 19980811
ZA 9808508 A	ZA 1998-8508 19980917
PH 1199802410 B1	PH 1999-2410 19990916
US 6465689 B1	US 1999-445633 19991208
HU 2000004582 A2	HU 2000-4582 19980811
JP 2001516738 W	JP 2000-511737 19980811
MX 218160 B	MX 2000-63 20000103
MX 2000000063 A1	MX 2000-63 20000103
KR 2001024079 A	KR 2000-702825 20000317
KR 563894 B1	KR 2000-702825 20000317
NO 2000001404 A	NO 2000-1404 20000317
JP 3878809 B2	WO 1998-US16652 19980811
JP 3878809 B2	JP 2000-511737 19980811

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 752444	B	Previous Publ	AU 9887791	A
DE 69814420	E	Based on	EP 1015415	A
ES 2197493	T3	Based on	EP 1015415	A
KR 563894	B1	Previous Publ	KR 2001024079	A
AU 9887791	A	Based on	WO 9914184	A
EP 1015415	A1	Based on	WO 9914184	A
BR 9812351	A	Based on	WO 9914184	A
HU 2000004582	A2	Based on	WO 9914184	A
JP 2001516738	W	Based on	WO 9914184	A
NZ 502786	A	Based on	WO 9914184	A
US 6465689	B1	Based on	WO 9914184	A
AU 752444	B	Based on	WO 9914184	A
EP 1015415	B1	Based on	WO 9914184	A
DE 69814420	E	Based on	WO 9914184	A
CA 2295993	C	Based on	WO 9914184	A
MX 218160	B	Based on	WO 9914184	A
KR 563894	B1	Based on	WO 9914184	A
JP 3878809	B2	Previous Publ	JP 2001516738	W
JP 3878809	B2	Based on	WO 9914184	A

PRIORITY APPLN. INFO: US 1997-59204P 19970918
US 1999-445633 19991208
MX 2000-63 20000103

AN 1999-254361 [21] WPIX

AB WO 1999014184 A1 UPAB: 20060115

NOVELTY - Stereoselective preparation of **gabapentin** (I) from cyclohexanone and triethylphosphonoacetate, involves reducing a nitro ester intermediate to produce a lactam and heating.

DETAILED DESCRIPTION - Preparation of **gabapentin** (1-aminomethylcyclohexane-1-acetic acid) of formula (I) comprises: (1) adding cyclohexanone to a mixture of sodium hydride suspended in dry tetrahydrofuran (THF) to which triethyl phosphonoacetate is added;
(2) partitioning the mixture between HCl and diethyl ether and collecting the ether layer;
(3) dissolving the obtained alpha,beta-unsaturated ester in THF with nitromethane and tetrabutylammonium fluoride (Bu4NF) and heating;
(4) dissolving the obtained nitro ester in methanol and shaking over a catalyst and
(5) heating the obtained lactam to reflux in mixture of HCl and dioxan to give (I) and optionally converting (I) to a salt. INDEPENDENT CLAIMS are also included for the following: (A) preparation of a **gabapentin** derivative of formula (II) which comprises:
(a) adding 4-methylcyclohexanone to a mixture of sodium hydride suspended in dry THF to which triethyl phosphonoacetate is added;
(b) decanting the solvent from the obtained mixture; (c) dissolving the obtained alpha,beta-unsaturated ester in nitromethane and heating the obtained mixture and (d) heating the obtained product to reflux in a mixture HCl and dioxan to give (II) and optionally converting (II) to a salt and (B) preparation of **gabapentin** derivatives of

formula (III) and (IV) as in process (A) starting from cis-3,5-dimethylcyclohexanone and 3R 3-methylcyclohexanone, respectively.
ACTIVITY - Antiepileptic.
USE - **Gabapentin** is used in the treatment of epilepsy.
ADVANTAGE - The process is stereoselective and gives stereochemical control and high stereochemical purity. Resolution is not required.

L43 ANSWER 22 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:172984 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300172984
TITLE: Process for producing **gabapentin** or pharmaceutical grade.
AUTHOR(S): Bosch Llado, Jordi [Inventor, Reprint Author]; Onrubia Miguel, Ma del Carmen [Inventor]; Pagans Lista, Eugenia [Inventor]
CORPORATE SOURCE: Girona, Spain
ASSIGNEE: Medichem, S.A., Barcelona, Spain
PATENT INFORMATION: US 6528682 20030304
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar 4 2003) Vol. 1268, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Apr 2003
Last Updated on STN: 2 Apr 2003
AB The invention describes a process for the preparation of pharmaceutical grade **gabapentin**, consisting of neutralizing an alcoholic solution of **gabapentin hydrochloride** with basic ion exchange resins and thereafter directly isolating the **gabapentin**, without requiring either the formation or the isolation of intermediates other than the pharmaceutical grade product.

L43 ANSWER 23 OF 26 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:451660 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200451660
TITLE: Experimental conditions for the continuous subcutaneous infusion of four central analgesics in rats.
AUTHOR(S): Slot, L. A. Bruins [Reprint author]; Tarayre, J.-P.; Koek, W.; Ribet, J.-P.; Colpaert, F. C.
CORPORATE SOURCE: Centre de Recherche Pierre Fabre 17, Avenue Jean Moulin, 81106, Castres Cedex, France
liesbeth.bruins.slot@pierre-fabre.com
SOURCE: Pharmacology Biochemistry and Behavior, (July, 2002) Vol. 72, No. 4, pp. 943-951. print.
CODEN: PBBHAU. ISSN: 0091-3057.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Aug 2002
Last Updated on STN: 23 Sep 2002
AB For the analysis of pharmacotherapeutic regimens for chronic pain in animals, it is important to establish delivery methods in which analgesics can be administered continuously and at a constant rate for a prolonged period of time. This allows for the assessment of how drug effects may vary over time in the presence of ongoing pain. The present study determined, for four analgesic compounds, the maximal doses that met all of the following criteria: (i) water-soluble, (ii) stable over 14 days at 38 degreeC, and (iii) devoid of undesirable side-effects in normal rats, as assessed by evolution of body weight and temperature after the subcutaneous implantation of an osmotic mini-pump that continuously infused the compounds over a 14-day period. The results showed the maximal doses to be 5 mg/rat/day for morphine hydrochloride, 2.5 mg/rat/day for imipramine hydrochloride, 20 mg/rat/day for ketamine hydrochloride, and 10 mg/rat/day for **gabapentin**. These doses were further found to be sufficient to

express each compound's representative pharmacological activity. The conditions identified here appear appropriate for future studies of these four compounds in rat models of chronic pain and neuropathic allodynia.

L43 ANSWER 24 OF 26 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:46265 CASREACT Full-text
TITLE: Preparation of gabapentin from gabapentin hydrochloride
INVENTOR(S): Chen, Shiming; Shi, Desong
PATENT ASSIGNEE(S): Zhejiang Jiuzhou Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1683322	A	20051019	CN 2005-10049346	20050311

PRIORITY APPLN. INFO.: CN 2005-10049346 20050311
AB The title method includes (1)dissolving gabapentin hydrochloride in methanol, ethanol, absolute methanol or absolute ethanol as solvent; neutralizing with sodium or potassium salt of the solvent till pH value of 6.9-7.2, stirring, heating to reflux, cooling, filtering, and recovering the solvent under reduced pressure till all the material becomes solid; (2) dissolving the solid with methanol or ethanol under heat, refluxing, cooling, and crystallizing to obtain gabapentin crude product; (3) heating and dissolving the crude product with absolute methanol or absolute ethanol, cooling, filtering, condensing the filtrate, cooling, crystallizing, filtering, and washing to obtain the gabapentin.

L43 ANSWER 25 OF 26 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:153102 CASREACT Full-text
TITLE: Method for preparing gabapentin
INVENTOR(S): Cao, Guidong
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1539815	A	20041027	CN 2003-10108375	20031030

PRIORITY APPLN. INFO.: CN 2003-10108375 20031030
AB A process is disclosed for preparing gabapentin from gabapentin hydrochloride which includes dissolving gabapentin hydrochloride in ion exchanging water, regulating pH = 7.14-8, stirring, heating to just below 60°C by water bath, vacuum concentrating to become solid, adding organic solvent, vacuum distilling, thermally dissolving anhydrous organic solvent, cooling, filtering, distilling the filtrate for drying, dissolving in absolute alc., refluxing, cooling for crystallizing coarse gabapentin, dissolving in absolute alc., cooling, filtering concentrating, cooling for crystallizing, filtering and washing with absolute alc.

L43 ANSWER 26 OF 26 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 114:229385 CASREACT Full-text
TITLE: Process for the preparation of 1-aminomethyl-1-cyclohexaneacetic acid (gabapentin)
INVENTOR(S): Geibel, Wolfram; Hartenstein, Johannes; Herrmann, Wolfgang; Witzke, Joachim
PATENT ASSIGNEE(S): Goedecke A.-G., Germany
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 414274	A2	19910227	EP 1990-116292	19900824
EP 414274	A3	19910515		
EP 414274	B1	19930623		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 3928182	A1	19910228	DE 1989-3928182	19890825
US 5091567	A	19920225	US 1990-570487	19900821
IL 95479	A	19960912	IL 1990-95479	19900823
HU 54623	A2	19910328	HU 1990-5332	19900824
HU 207284	B	19930329		
JP 03118355	A	19910520	JP 1990-221421	19900824
JP 2846084	B2	19990113		
AT 90936	T	19930715	AT 1990-116292	19900824
ES 2058707	T3	19941101	ES 1990-116292	19900824
FI 103040	B	19990415	FI 1990-4203	19900824
FI 103040	B1	19990415		
PRIORITY APPLN. INFO.:			DE 1989-3928182	19890825
			EP 1990-116292	19900824

AB The title compound (I) was prepared by 1) reaction of cyclohexanone, KOH, and a phosphonate to give a cyclohexylideneacetate, 2) condensation of the latter with MeNO2 using alkali metal carbonate/Me2SO to give 1-nitromethylcyclohexaneacetate, 3) reduction of the latter to 1-aminomethylcyclohexaneacetate and 2-azaspiro[4,5]decan-3-one at >100°, 4) treatment of the latter with diluted HCl to give I.HCl salt, and 5) treatment of the salt with ion exchange resin. Thus, cyclohexanone and tri-Et phosphonoacetate were added successively to KOH in THF at room temperature to give 94.3% Et cyclohexylideneacetate. The latter and MeNO2 were added to K2CO3 in Me2SO at 95° to give 89.4% Et 1-(nitromethyl)cyclohexaneacetate. This was hydrogenated in EtOH over Pd/C at 125° to give 91.6% 2-azaspiro[4.5]decan-3-one which was refluxed with dilute HCl to give 64.7% I.HCl, and converted to I free base via ion exchange.

=> file hcaplus medline biosis embase wpix japio jicst
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FILE 'MEDLINE' ENTERED AT 17:56:27 ON 21 MAR 2007

FILE 'BIOSIS' ENTERED AT 17:56:27 ON 21 MAR 2007

FILE 'EMBASE' ENTERED AT 17:56:27 ON 21 MAR 2007

FILE 'WPIX' ENTERED AT 17:56:27 ON 21 MAR 2007

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FILE 'JAPIO' ENTERED AT 17:56:27 ON 21 MAR 2007
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FILE 'JICST-EPLUS' ENTERED AT 17:56:27 ON 21 MAR 2007
COPYRIGHT (C) 2007 Japan Science and Technology Agency (JST)

L36          14 SEA ABB=ON  PLU=ON  "KUPPUSWAMY N"?/AU
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L38           6 SEA ABB=ON  PLU=ON  "MARIADAS A"?/AU
L39           4 SEA ABB=ON  PLU=ON  L36 AND L37 AND L38
L40           8 SEA ABB=ON  PLU=ON  L36 AND (L37 OR L38)
L41           4 SEA ABB=ON  PLU=ON  L36 AND L38
L42           8 SEA ABB=ON  PLU=ON  L39 OR L40 OR L41

=> dup rem l42
PROCESSING COMPLETED FOR L42
L44           4 DUP REM L42 (4 DUPLICATES REMOVED)
                ANSWERS '1-4' FROM FILE HCAPLUS

=> d l44 1-4 ibib abs

L44  ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2005:1026923  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:286690
TITLE:                    Synthesis of 4-tert-butylgabapentin
INVENTOR(S):              Kuppuswamy, Nagarajan; Hariharan,
                          Sivaramakrishnan; Iyer, Venkatachalam
                          Shankar; Balakrishnan, Suresh Babu;
                          Krishnamurthi, Gopalakrishnan; Kuppana, Ananda;
                          Karuppiah, Muruga Poopati Raja; Padmanabhan,
                          Balaram; Subrayashastry, Aravinda; Prema,
                          Gouriamma Vasudev; Narayanaswamy, Shamala
PATENT ASSIGNEE(S):       Hikal Limited, India; Indian Institute of
                          Science
SOURCE:                   PCT Int. Appl., 17 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     WO 2005087709         A1    20050922    WO 2005-IN82
                                                                     200503
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         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
             MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,
             SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US,
             UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
             DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC,
             NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2570255            A1    20050922    CA 2005-2570255
                                                                     200503
                                                                     16
PRIORITY APPLN. INFO.:                       US 2004-553565P      P
                                                                     200403
                                                                     17

                                             WO 2005-IN82         W
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200503
16

AB The invention relates to a process for the preparation of the cis (Z) and trans (E) stereoisomers of 4-tert-butylgabapentin. 4-Tert-butylgabapentin as a mixture of stereoisomers was prepared by treating 4-tert-butylcyclohexanone with Et cyanoacetate and ammonia in methanol, hydrolysis of the dicyano imide product with hot sulfuric acid, conversion to the anhydride, treatment with aqueous ammonia to give the monoamide as a mixture of approx. equal proportions of stereoisomers, reaction with NaOBr to form the lactam, hydrolysis of the lactam with hot concentrated HCl, and neutralization with aqueous NaOH to pH 7. The stereoisomers of 4-tert-butylgabapentin were separated by fractional crystallization from aqueous methanol.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2005:1026620 HCAPLUS Full-text
DOCUMENT NUMBER: 143:267241
TITLE: Preparation of gabapentin analogues
INVENTOR(S): **Kuppuswamy, Nagarajan; Hariharan, Sivaramakrishnan**; Iyer, Venkatachalam Sankar; Balakrishnan, Suresh Babu; Krishnamurthi, Gopalakrishnan; Kuppanna, Ananda; Karuppiah, Muruga Poopati Raja; Padmanabhan, Balaram; Subrayashastry, Aravinda; Prema, Gouriamma Vasudev; Narayanaswamy, Shamala
PATENT ASSIGNEE(S): Hikal Limited, India; Indian Institute of Science
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005209332	A1	20050922	US 2005-79481	200503 15
PRIORITY APPLN. INFO.:			US 2004-553565P P	200403 17

OTHER SOURCE(S): CASREACT 143:267241
AB The invention relates to a process for the preparation of the cis (Z) and trans (E) stereoisomers of 4-tert-butylgabapentin. 4-Tert-butylgabapentin as a mixture of stereoisomers was prepared by treating 4-tert-butylcyclohexanone with Et cyanoacetate and ammonia in methanol, hydrolysis of the dicyano imide product with hot sulfuric acid, conversion to the anhydride, treatment with aqueous ammonia to give the monoamide as a mixture of approx. equal proportions of stereoisomers, reaction with NaOBr to form the lactam, hydrolysis of the lactam with hot concentrated HCl, and neutralization with aqueous NaOH to pH 7. The stereoisomers of 4-tert-butylgabapentin were separated by fractional crystallization from aqueous methanol.

L44 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:453184 HCAPLUS Full-text
DOCUMENT NUMBER: 141:7020
TITLE: An improved process for the preparation of gabalactam by Hofmann reaction in the presence of bromine and alkali or alkaline hydroxides
INVENTOR(S): **Kuppuswamy, Nagarajan; Hariharan, Sivaramakrishnan; Mariadas, Arulselvan**

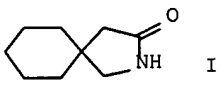
PATENT ASSIGNEE(S): Hikal Ltd., India
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004046108	A1	20040603	WO 2002-IN225	200211 20
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506564	A1	20040603	CA 2002-2506564	200211 20
AU 2002356427	A1	20040615	AU 2002-356427	200211 20
EP 1599446	A1	20051130	EP 2002-808153	200211 20
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2006135789	A1	20060622	US 2006-535278	200602 15

PRIORITY APPLN. INFO.: WO 2002-IN225 W 200211 20

OTHER SOURCE(S): CASREACT 141:7020

GI



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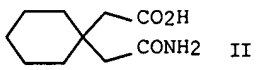

II

AB The invention is related to an improved process for the preparation of highly pure gabalactam (I, gabapentin-lactam, 2-azaspiro[4,5]decan-3- one), useful in the synthesis of gabapentin, by Hofmann reaction of amide II in the presence of an alkali or alkaline earth hypobromite (5-10 weight %) generated from Br2 and the corresponding hydroxide, e.g. NaOH. The advantages include elimination of toxic reagents and pyrophoric

catalysts, use of low cost materials, and purity of gabalactam > 95%. The claims and examples describe the reaction conditions and purification of I.

L44 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2004:453164 HCAPLUS Full-text
DOCUMENT NUMBER: 140:423950
TITLE: Process for the preparation of (aminomethyl)cycloalkaneacetic acids
INVENTOR(S): **Kuppuswamy, Nagarajan; Hariharan, Sivaramakrishnan; Mariadas, Arulselvan**
PATENT ASSIGNEE(S): Hikal Ltd., India
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004046085	A1	20040603	WO 2002-IN224	200211 20
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506563	A1	20040603	CA 2002-2506563	200211 20
AU 2002356426	A1	20040615	AU 2002-356426	200211 20
EP 1603863	A1	20051214	EP 2002-808152	200211 20
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2006149099	A1	20060706	US 2003-535253	200602 09

PRIORITY APPLN. INFO.: WO 2002-IN224 W 200211 20

OTHER SOURCE(S): CASREACT 140:423950; MARPAT 140:423950

AB The invention relates to an improved process for the preparation of (aminomethyl)cycloalkaneacetic acids, in particular gabapentin (1-aminomethyl-1-cyclohexaneacetic acid). The claims and examples describe the neutralization of gabapentin hydrochloride with an aqueous solution of an alkali metal base (40-50 weight %).

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=> d his full

     (FILE 'HOME' ENTERED AT 12:19:11 ON 21 MAR 2007)

     FILE 'REGISTRY' ENTERED AT 12:19:19 ON 21 MAR 2007
L1             1 SEA ABB=ON  PLU=ON  GABAPENTIN/CN
L2             1 SEA ABB=ON  PLU=ON  GABAPENTIN HYDROCHLORIDE/CN
L3             1 SEA ABB=ON  PLU=ON  SODIUM HYDROXIDE/CN
L4             1 SEA ABB=ON  PLU=ON  POTASSIUM HYDROXIDE/CN
L5             1 SEA ABB=ON  PLU=ON  LITHIUM HYDROXIDE/CN
L6             3 SEA ABB=ON  PLU=ON  L3 OR L4 OR L5
L7             1 SEA ABB=ON  PLU=ON  METHANOL/CN
L8             1 SEA ABB=ON  PLU=ON  ISOPROPYL ALCOHOL/CN
L9             1 SEA ABB=ON  PLU=ON  TOLUENE/CN
L10            1 SEA ABB=ON  PLU=ON  ETHYLENE DICHLORIDE/CN
L11            1 SEA ABB=ON  PLU=ON  METHYLENE DICHLORIDE/CN
L12            1 SEA ABB=ON  PLU=ON  HEXANE/CN
L13            6 SEA ABB=ON  PLU=ON  L7 OR L8 OR L9 OR L10 OR L11 OR L12

     FILE 'HCAPLUS' ENTERED AT 12:25:06 ON 21 MAR 2007
L14         1890 SEA ABB=ON  PLU=ON  L1 OR GABAPENTIN OR NEURONTIN
L15           70 SEA ABB=ON  PLU=ON  L2 OR GABAPENTIN (W) (HCL OR
                 HYDROCHLORIDE OR (HYDROGEN OR H) (W) (CL OR CHLORIDE))
L16              QUE ABB=ON  PLU=ON  L6 OR (NA OR K OR LI OR LITHIUM OR
                 SODIUM OR POTASSIUM) (W) (OH OR HYDROXIDE) OR NAOH OR
                 KOH OR LIOH OR ALKALI METAL BASE
L17           67 SEA ABB=ON  PLU=ON  L14 AND L15
L18           16 SEA ABB=ON  PLU=ON  L14 AND L15 AND L16
L19           10 SEA ABB=ON  PLU=ON  L18 AND (1840-2002)/PRY,PY,AY

     FILE 'WPIX' ENTERED AT 17:07:47 ON 21 MAR 2007
L20          532 SEA ABB=ON  PLU=ON  GABAPENTIN OR NEURONTIN
L21           39 SEA ABB=ON  PLU=ON  GABAPENTIN (W) (HCL OR HYDROCHLORIDE
                 OR (HYDROGEN OR H) (W) (CL OR CHLORIDE))
L22              QUE ABB=ON  PLU=ON  (NA OR K OR LI OR LITHIUM OR SODIUM
                 OR POTASSIUM) (W) (OH OR HYDROXIDE) OR NAOH OR KOH OR
                 LIOH OR ALKALI METAL BASE
L23           39 SEA ABB=ON  PLU=ON  L20 AND L21
L24           18 SEA ABB=ON  PLU=ON  L20 AND L21 AND L22
L25           11 SEA ABB=ON  PLU=ON  L23 AND (C07C0227 OR A61K000)/IC
L26           21 SEA ABB=ON  PLU=ON  L24 OR L25

     FILE 'JAPIO' ENTERED AT 17:14:53 ON 21 MAR 2007
L27            0 SEA ABB=ON  PLU=ON  L20 AND L21

     FILE 'EMBASE' ENTERED AT 17:15:26 ON 21 MAR 2007
L28            0 SEA ABB=ON  PLU=ON  L20 AND L21

     FILE 'BIOSIS' ENTERED AT 17:15:40 ON 21 MAR 2007
L29            2 SEA ABB=ON  PLU=ON  L20 AND L21
L30            0 SEA ABB=ON  PLU=ON  L20 AND L21 AND L22

     FILE 'JICST-EPLUS' ENTERED AT 17:16:30 ON 21 MAR 2007
L31            0 SEA ABB=ON  PLU=ON  L20 AND L21

     FILE 'MEDLINE' ENTERED AT 17:16:58 ON 21 MAR 2007
L32            0 SEA ABB=ON  PLU=ON  L20 AND L21

     FILE 'CASREACT' ENTERED AT 17:17:23 ON 21 MAR 2007
L33           16 SEA ABB=ON  PLU=ON  L1/PRO
L34            7 SEA ABB=ON  PLU=ON  L2/RRT
L35            6 SEA ABB=ON  PLU=ON  L33 AND L34

     FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, JICST-EPLUS'
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     ENTERED AT 17:29:55 ON 21 MAR 2007
L36           14 SEA ABB=ON  PLU=ON  "KUPPUSWAMY N"?/AU
L37          652 SEA ABB=ON  PLU=ON  "HARIHARAN S"?/AU
L38            6 SEA ABB=ON  PLU=ON  "MARIADAS A"?/AU
L39            4 SEA ABB=ON  PLU=ON  L36 AND L37 AND L38
L40            8 SEA ABB=ON  PLU=ON  L36 AND (L37 OR L38)
L41            4 SEA ABB=ON  PLU=ON  L36 AND L38
L42            8 SEA ABB=ON  PLU=ON  L39 OR L40 OR L41

     FILE 'WPIX, BIOSIS, CASREACT' ENTERED AT 17:54:25 ON 21 MAR 2007
L43           26 DUP REM L26 L29 L35 (3 DUPLICATES REMOVED)
                    ANSWERS '1-21' FROM FILE WPIX
                    ANSWERS '22-23' FROM FILE BIOSIS
                    ANSWERS '24-26' FROM FILE CASREACT
                D L43 1-26 IBIB ABS

     FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, JICST-EPLUS'
     ENTERED AT 17:56:27 ON 21 MAR 2007
L44            4 DUP REM L42 (4 DUPLICATES REMOVED)
                    ANSWERS '1-4' FROM FILE HCAPLUS
                D L44 1-4 IBIB ABS


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   19 MAR 2007  HIGHEST RN 927525-36-8
     DICTIONARY FILE UPDATES:  19 MAR 2007  HIGHEST RN 927525-36-8

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For informatio
     on property searching in REGISTRY, refer to:

     http://www.cas.org/ONLINE/UG/regprops.html

     FILE HCAPLUS

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     FILE COVERS 1907 - 21 Mar 2007  VOL 146 ISS 13
     FILE LAST UPDATED: 20 Mar 2007  (20070320/ED)

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

      This file contains CAS Registry Numbers for easy and accurate
      substance identification.

     FILE WPIX
```

FILE LAST UPDATED: 19 MAR 2007 <20070319/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200719 <200719/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<

>>> New display format FRAGHITSTR available <<<
SEE ONLINE NEWS and
http://www.stn-international.de/archive/stn_online_news/fraghitstr_e

>>> IPC Reform backfile reclassification has been loaded to 31 Decem 2006. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC. <<<

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http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

FILE JAPIO
FILE LAST UPDATED: 5 FEB 2007 <20070205/UP>
FILE COVERS APRIL 1973 TO OCTOBER 26, 2006

>>> GRAPHIC IMAGES AVAILABLE <<<

FILE EMBASE
FILE COVERS 1974 TO 21 Mar 2007 (20070321/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 14 March 2007 (20070314/ED)

FILE JICST-EPLUS
FILE COVERS 1985 TO 19 MAR 2007 (20070319/ED)

The database producer has informed us that as of March 31, 2007, the will no longer provide updates for the JICST-EPLUS file. Therefore, effective March 31, 2007, JICST-EPLUS will be removed from STN.

FILE MEDLINE
FILE LAST UPDATED: 17 Mar 2007 (20070317/UP). FILE COVERS 1950 TO

All regular MEDLINE updates from November 15 to December 16 have b

added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R and 2007 tree numbers.

The annual reload will be available in early 2007.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE CASREACT

FILE CONTENT:1840 - 17 Mar 2007 VOL 146 ISS 12

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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* CASREACT now has more than 12 million reactions *
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Some CASREACT records are derived from the ZIC/VINITI database (1974 provided by InfoChem, INPI data prior to 1986, and Biotransformation database compiled under the direction of Professor Dr. Klaus Kieslic

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